09/8/04 246.

Freeform Search

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Term: L6 and opposite

Display: 10 **Documents in Display Format:** - **Starting with Number** 1

Generate: ○ Hit List ◉ Hit Count ○ Side by Side ○ Image

Search | Clear | Interrupt

Search History

DATE: Tuesday, January 13, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L7	L6 and opposite	1	L7
L6	L5 and charge$2	1	L6
L5	L4 and biotin and streptavidin	1	L5
L4	L1 and captur$3	1	L4
L3	l1 and opposite charge$1	0	L3
L2	L1 and (opposite charge$2 near5 captur$3)	0	L2
L1	6214388.pn.	2	L1

END OF SEARCH HISTORY

First Hit Fwd Refs

End of Result Set

L7: Entry 2 of 2 File: USPT Oct 17, 1995

DOCUMENT-IDENTIFIER: US 5459078 A
TITLE: Methods and reagents for performing ion-capture digoxin assays

Brief Summary Text (25):
Other assay methods involve the use of auxiliary specific binding members. Tanswell et al. (U.S. Pat. No. 4,624,930) describe a process for determining the presence of a polyvalent antigen by incubating the antigen with three receptors; a first and a third receptor which bind to the antigen and a second receptor, bound to a solid support, which specifically binds to the first receptor. Valkirs et al. (U.S. Pat. No. 4,727,019) describe a method and device for ligand-receptor assays, as in Tanswell et al., wherein an anti-receptor (e.g., avidin) is immobilized on a porous member and binds to a receptor (e.g., an analyte-specific antibody bound to biotin) which is bound to the target ligand. Wolters et al. (U.S. Pat. No. 4,343,896) describe the use of ancillary specific binding members to prepare or complete detectable complexes, i.e., the use of a third antibody in a binding assay to complete a detectable analyte-binding member complex. W. Georghegan (U.S. Pat. No. 4,880,751) describes a method for preparing an immunoadsorption matrix by adsorbing the F(c) portion of a selected IgG molecule onto a charged surface. Parikh et al. (U.S. Pat. No. 4,298,685) describe the use of a conjugate of biotin and an anti-analyte antibody together with an inert support bearing immobilized avidin. The specific binding of the avidin and biotin components enables the immobilization of the antibody on the inert support.

Brief Summary Text (42):
The term "specific binding member", as used herein, refers to a member of a specific binding pair, i.e., two different molecules where one of the molecules through chemical or physical means specifically binds to the second molecule. The complementary members of a specific binding pair may also be referred to as a ligand and a receptor. In addition to the well-known example of the antigen and antibody specific binding pair, alternative specific binding pairs are exemplified by the following: biotin and avidin, carbohydrates and lectins, complementary nucleotide sequences (including probe and capture nucleic acid sequences used in DNA hybridization assays to detect a target nucleic acid sequence), complementary peptide sequences (including those formed by recombinant methods), effector and receptor molecules, hormone and hormone binding protein, enzyme cofactors and enzymes, enzyme inhibitors and enzymes, and the like. Furthermore, specific binding pairs can include members that are analogs of the original specific binding member. For example, a derivative or fragment of the analyte (an analyte-analog) can be used so long as it has at least one epitope in common with the analyte. Immunoreactive specific binding members include antigens, haptens, antibodies, and complexes thereof including those formed by recombinant DNA methods or peptide synthesis. An antibody can be a monoclonal or polyclonal antibody, a chimeric antibody, a recombinant protein or a mixture(s) or fragment(s) thereof, as well as a mixture of an antibody and other specific binding members. The details of the preparation of such antibodies and their suitability for use as specific binding members are well-known to those skilled-in-the-art.

Brief Summary Text (90):
In general, once complex formation occurs between the analyte and the assay reagents, the oppositely charged solid phase is used as a separation mechanism: the

homogeneous reaction mixture is contacted with the solid phase, and the newly formed binding complexes are retained on the solid phase through the interaction of the opposite charges of the solid phase and the capture reagent. If the user is not concerned with liquid phase kinetics, the capture reagent can be pre-immobilized on the solid phase to form a capture site.

CLAIMS:

1. A competitive assay method for determining the presence or amount of digoxin in a test sample, comprising the sequential steps of:

a) providing

(i) a soluble capture reagent comprising a binding member conjugated through a single point of covalent attachment to a polymeric anion having a net negative charge under specific binding assay conditions, wherein said binding member is selected from the group consisting of (1) an anti-digoxin antibody and (2) a binding member which specifically binds an ancillary antibody which specifically binds digoxin,

(ii) an indicator reagent comprising (1) digoxin and a detectable label or (2) a digoxin analog and a detectable label,

(iii) a solid phase material containing a reaction site comprising a polymeric cation having a net negative charge under specific binding assay conditions and having a nitrogen content of about two to about ten percent excluding counter ions, and

(iv) when said soluble capture reagent comprises said binding member which specifically binds said ancillary antibody, further providing said ancillary antibody;

b) contacting said solid phase with said capture reagent, said test sample, and said ancillary antibody when said capture reagent comprises said binding member which specifically binds said ancillary antibody, thereby forming (1) capture reagent/digoxin complex or (2) capture reagent/ancillary antibody/digoxin complex with any digoxin present in said test sample, and immobilizing both unreacted capture reagent and said complex comprising reacted capture reagent on said solid phase by ionic interaction of the oppositely charged polymeric anion and polymeric cation;

c) contacting said solid phase with said indicator reagent to specifically bind said indicator reagent to said immobilized unreacted capture reagent in inverse proportion to the amount of said digoxin present in said test sample; and

d) detecting said indicator reagent bound to said solid phase to determine the presence or amount of said digoxin in said test sample.

12. A competitive assay method for determining the presence or amount of digoxin in a test sample, comprising the sequential steps of:

a) providing

(i) a soluble capture reagent comprising a binding member conjugated through a single point of covalent attachment to a polymeric anion having a net negative charge under specific binding assay conditions, wherein said binding member is selected from the group consisting of (1) an anti-digoxin antibody and (2) a binding member which specifically binds an ancillary antibody which specifically binds digoxin,

(ii) an indicator reagent comprising (1) digoxin and a detectable label or (2) a digoxin analog and a detectable label,

(iii) a solid phase material containing a reaction site comprising a polymeric cation having a net negative charge under specific binding assay conditions and having a nitrogen content of about two to about ten percent excluding counter ions, and

when said soluble capture reagent comprises said binding member which specifically binds said ancillary antibody, further providing said ancillary antibody;

b) contacting said solid phase with said capture reagent, said indicator reagent said test sample, and said ancillary antibody when said capture reagent comprises said binding member which specifically binds said ancillary antibody, thereby forming (1) capture reagent/digoxin complex or (2) capture reagent/ancillary antibody/digoxin complex with any digoxin present in said test sample, and immobilizing both unreacted capture reagent and said complex comprising reacted capture reagent on said solid phase by ionic interaction of the oppositely charged polymeric anion and polymeric cation, and specifically binding said indicator reagent to said

immobilized unreacted capture reagent in inverse proportion to the amount of said digoxin present in said test sample; and

c) detecting bound or unbound indicator reagent to determine the presence or amount of said digoxin in said test sample.

17. A sandwich assay method for determining the presence or amount of digoxin in a test sample, comprising the sequential steps of:

a) providing

(i) a soluble capture reagent, comprising (1) digoxin or a digoxin analog, conjugated through a single point of covalent attachment to (2) polymeric anion having a net negative charge under specific binding assay conditions,

(ii) an indicator reagent, comprising a binding member and a detectable label, wherein said binding member is selected from the group consisting of (1) an anti-digoxin antibody and (2) a binding member which specifically binds an ancillary antibody which specifically binds digoxin,

(iii) a solid phase material containing a reaction site comprising a polymeric cation having a net negative charge under specific binding assay conditions and having a nitrogen content of about two to about ten percent excluding counter ions, and

(iv) when said indicator reagent comprises said binding member which specifically binds said ancillary antibody, further providing said ancillary antibody;

b) contacting said capture reagent, said indicator reagent and said test sample, and said ancillary antibody when said indicator reagent comprises said binding member which specifically binds said ancillary antibody, thereby forming a mixture, and then incubating said mixture to form (1) capture reagent/indicator reagent complex or (2) capture reagent/ancillary antibody/indicator reagent complex in inverse proportion to the amount of said digoxin present in said test sample, and contacting said mixture with said solid phase, whereby unreacted capture reagent and said complexes comprising capture reagent are immobilized on said solid phase by ionic interaction of the oppositely charged polymeric anion and polymeric cation; and

c) detecting indicator reagent (1) bound to the digoxin in the test sample or (2) indicator reagent bound to the digoxin or digoxin analog in said complex to determine the presence or amount of said digoxin in said test sample.

20. An assay method for determining the presence or amount of digoxin in a test sample, comprising the sequential steps of:

a) providing

(i) a soluble capture reagent, comprising a first binding member selected from the group consisting of (1) an anti-digoxin antibody and (2) a binding member which specifically binds an ancillary antibody which specifically binds digoxin, conjugated through a single point of covalent attachment to a first polymeric anion of the formula ##STR11## wherein n is about 10 to about 500; z is about 1 to about 6; W is H.sup.+, Na.sup.+, K.sup.+, Li.sup.+, amine salts and derivatives thereof; and X provides said single point of covalent attachment and is an amine-reactive group or moiety, a thiol-reactive group or moiety, or a thiol group or moiety represented by --A--SH wherein A is a spacer arm; said first polymeric anion having a net negative charge under specific binding assay conditions,

(ii) an indicator reagent, comprising (1) a second binding member which specifically binds to digoxin and (2) a detectable label,

(iii) a non-specific binding blocker comprising a second unbound polymeric anion selected from the group consisting of dextran sulfate, heparin, carboxymethyl dextran, carboxymethyl cellulose, pentosan polysulfate, inositol hexasulfate, and Beta-cyclodextrin sulfate,

(iv) a solid phase material containing a reaction site comprising a polymeric cation having a net negative charge under specific binding assay conditions, wherein said non-specific binding blocker inhibits nonspecific binding to said indicator reagent to said solid phase, and

(v) when said capture reagent comprises said binding member which specifically binds said ancillary antibody, further providing said ancillary antibody;

b) sequentially or simultaneously contacting said solid phase, said capture reagent, said indicator reagent and said test sample, and said ancillary antibody when said capture reagent comprises said binding member which specifically binds said ancillary antibody, thereby (i) forming (1) capture reagent/digoxin complex or (2) capture reagent/ancillary antibody/digoxin complexes with any digoxin present in said test sample; (ii) immobilizing both unreacted capture reagent and said complex comprising reacted capture reagent on said solid phase by ionic interaction of the oppositely charged said first polymeric anion and said polymeric cation; and (iii) specifically binding said indicator reagent to said immobilized complex comprising reacted capture reagent in proportion to the amount of the digoxin present in the sample; and

c) detecting said indicator reagent bound to said solid phase to determine the presence or amount of said digoxin in said test sample.

29. An assay method for determining the presence or amount of digoxin in a test sample, comprising the sequential steps of:

a) providing

(i) a soluble capture reagent, comprising a first binding member selected from the group consisting of (1) an anti-digoxin antibody and (2) a binding member which specifically binds an ancillary antibody which specifically binds digoxin, said first binding member conjugated through a single point of covalent attachment to a

first polymeric anion having a net negative charge under specific binding assay conditions,

(ii) an indicator reagent, comprising (1) a second binding member which specifically binds to digoxin and (2) detectable label, and

(iii) a solid phase material containing a reaction site comprising a polymeric cation having a net negative charge under specific binding assay conditions and having a nitrogen content of about two to about ten percent excluding counter ions, and

(iv) when said capture reagent comprises said binding member which specifically binds said ancillary antibody, further providing said ancillary antibody;

b) contacting said solid phase with said capture reagent, said test sample, and said ancillary antibody when said capture reagent comprises said binding member which specifically binds said ancillary antibody, thereby forming (1) capture reagent/digoxin complex or (2) capture reagent/ancillary antibody/digoxin complex with any digoxin present in said test sample, and immobilizing both unreacted capture reagent and said complex comprising reacted capture reagent on said solid phase by ionic interaction of the oppositely charged polymeric anion and polymeric cation;

c) contacting said solid phase with said indicator reagent to specifically bind said indicator reagent to said immobilized unreacted capture reagent or complexes comprising reacted capture reagent in direct proportion to the amount of said digoxin present in said test sample; and

d) detecting said indicator reagent bound to said solid phase to determine the presence or amount of said digoxin in said test sample.

09825 246

Freeform Search

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Term: L4 and (opposite$1 near5 charge$1)

Display: 10 **Documents in Display Format:** - **Starting with Number** 1

Generate: ○ Hit List ◉ Hit Count ○ Side by Side ○ Image

Search | Clear | Interrupt

Search History

DATE: Tuesday, January 13, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L5	L4 and (opposite$1 near5 charge$1)	2	L5
L4	(nucleic acid$1 or polynucleotide$1) near5 captur$3 near5 ligand$1	71	L4
L3	L2 and (ionic interact$3 or ionic captur$3)	4	L3
L2	L1 and (charge$1 or opposite$1)	79	L2
L1	(nucleic acid or polynucleotide) near5 captur$3 near5 (reagent$1 or agent$1)	147	L1

END OF SEARCH HISTORY

09/874,246

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
NEWS  2          "Ask CAS" for self-help around the clock
NEWS  3  SEP 09  CA/CAplus records now contain indexing from 1907 to the
                 present
NEWS  4  DEC 08  INPADOC: Legal Status data reloaded
NEWS  5  SEP 29  DISSABS now available on STN
NEWS  6  OCT 10  PCTFULL: Two new display fields added
NEWS  7  OCT 21  BIOSIS file reloaded and enhanced
NEWS  8  OCT 28  BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS  9  NOV 24  MSDS-CCOHS file reloaded
NEWS 10  DEC 08  CABA reloaded with left truncation
NEWS 11  DEC 08  IMS file names changed
NEWS 12  DEC 09  Experimental property data collected by CAS now available
                 in REGISTRY
NEWS 13  DEC 09  STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS 14  DEC 17  DGENE: Two new display fields added
NEWS 15  DEC 18  BIOTECHNO no longer updated
NEWS 16  DEC 19  CROPU no longer updated; subscriber discount no longer
                 available
NEWS 17  DEC 22  Additional INPI reactions and pre-1907 documents added to CAS
                 databases
NEWS 18  DEC 22  IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS 19  DEC 22  ABI-INFORM now available on STN

NEWS EXPRESS  DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT
              MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS INTER    General Internet Information
NEWS LOGIN    Welcome Banner and News Items
NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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FILE 'HOME' ENTERED AT 11:01:19 ON 13 JAN 2004

=> file medline caplus biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.63       0.63

FILE 'MEDLINE' ENTERED AT 11:03:07 ON 13 JAN 2004

FILE 'CAPLUS' ENTERED AT 11:03:07 ON 13 JAN 2004
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=> file embase
```

```
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         1.67       2.30

FILE 'EMBASE' ENTERED AT 11:03:13 ON 13 JAN 2004
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 FILE COVERS 1974 TO 5 Jan 2004 (20040105/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s captur###(10a)nucleic acid(10a)ligand#
         21826 CAPTUR###
         31324 "NUCLEIC"
       1190986 "ACID"
         26661 NUCLEIC ACID
                 ("NUCLEIC"(W)"ACID")
        116643 LIGAND#
L1           0 CAPTUR###(10A)NUCLEIC ACID(10A)LIGAND#

=> s captur###(10a)ligand###
         21826 CAPTUR###
        117554 LIGAND###
L2         104 CAPTUR###(10A)LIGAND###

=> s l2 and nucleic acid
         31324 "NUCLEIC"
       1190986 "ACID"
         26661 NUCLEIC ACID
                 ("NUCLEIC"(W)"ACID")
L3           0 L2 AND NUCLEIC ACID

=> s l2 and ionic interat###
         37121 "IONIC"
            71 INTERAT###
             1 IONIC INTERAT###
                 ("IONIC"(W)INTERAT###)
L4           0 L2 AND IONIC INTERAT###

=> s captur### (10a) ionic interact###
         21826 CAPTUR###
         37121 "IONIC"
        469138 INTERACT###
           348 IONIC INTERACT###
                 ("IONIC"(W)INTERACT###)
L5           0 CAPTUR### (10A) IONIC INTERACT###

=> s captur###(10a)opposite# (10a)charge#
         21826 CAPTUR###
         38028 OPPOSITE#
         61087 CHARGE#
L6           0 CAPTUR###(10A)OPPOSITE# (10A)CHARGE#

=> s ionic interact###
         37121 "IONIC"
        469138 INTERACT###
L7         348 IONIC INTERACT###
                 ("IONIC"(W)INTERACT###)

=> s l7 and ((captur### or attach###)(10a)ligand#)
         21826 CAPTUR###
```

```
         41728 ATTACH###
        116643 LIGAND#
           476 (CAPTUR### OR ATTACH###)(10A)LIGAND#
L8           0 L7 AND ((CAPTUR### OR ATTACH###)(10A)LIGAND#)

=> s l7 and ligand#
        116643 LIGAND#
L9          48 L7 AND LIGAND#

=> s l9 and (captur### or attach###)
         21826 CAPTUR###
         41728 ATTACH###
L10          1 L9 AND (CAPTUR### OR ATTACH###)

=> d l10 bib ab kwic

L10 ANSWER 1 OF 1  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
    on STN
AN  2000082918  EMBASE
TI  Microcalorimetric studies of interactions between proteins and hydrophobic
    ligands in hydrophobic interaction chromatography: Effects of
    ligand chain length, density and the amount of bound protein.
AU  Lin F.-Y.; Chen W.-Y.; Ruaan R.-C.; Huang H.-M.
CS  W.-Y. Chen, Department of Chemical Engineering, National Central
    University, Chung-Li 320, Taiwan,Province of China.
    t313165@twncu865.ncu.edu.tw
SO  Journal of Chromatography A, (2000) 872/1-2 (37-47).
    Refs: 65
    ISSN: 0021-9673  CODEN: JCRAEY
PUI S 0021-9673(99)01231-5
CY  Netherlands
DT  Journal; Article
FS  029     Clinical Biochemistry
LA  English
SL  English
AB  Using isothermal titration calorimetry (ITC), this investigation directly
    measured the adsorption enthalpies of proteins on various hydrophobic
    adsorbents. Various amounts of butyl and octyl groups were
    attached onto CM-Sepharose to form C4 and C8, two types of
    hydrophobic adsorbents. The adsorption enthalpies of both trypsinogen and
    .alpha.- chymotrypsinogen A were measured at 4.0 M NaCl and pH 10.0, in
    which most ionic interaction was suppressed. The
    adsorption isotherms of both proteins on various adsorbents were also
    measured, thus allowing us to calculate the Gibbs free energy and entropy
    of adsorption. Experimental results indicated that the adsorption of both
    proteins on butyl-containing adsorbents was exothermic, while their
    adsorption on octyl ones was endothermic. In addition, binding of both
    proteins with the butyl ligand is basically an adsorption
    process, while binding with the octyl ligand is adsorption and
    partition processes. Moreover, on both butyl or octyl, the adsorption
    enthalpy became increasingly positive as the ligand density
    increased, while the adsorption entropy became more positive as the alkyl
    chain length or density of the adsorbent increased. In addition, ITC was
    used to measure protein-protein interaction. The adsorption enthalpy of
    both proteins increased as the amount of bound protein increased, and the
    enthalpy increase of trypsinogen appeared to be higher than that of
    .alpha.-chymotrypsinogen A. This observation implies that protein-protein
    repulsion was stronger among trypsinogen molecules in the experiments. (C)
    2000 Elsevier Science B.V.
TI  Microcalorimetric studies of interactions between proteins and hydrophobic
    ligands in hydrophobic interaction chromatography: Effects of
    ligand chain length, density and the amount of bound protein.
AB  . . . investigation directly measured the adsorption enthalpies of
    proteins on various hydrophobic adsorbents. Various amounts of butyl and
```

octyl groups were **attached** onto CM-Sepharose to form C4 and C8, two types of hydrophobic adsorbents. The adsorption enthalpies of both trypsinogen and .alpha.- chymotrypsinogen A were measured at 4.0 M NaCl and pH 10.0, in which most **ionic interaction** was suppressed. The adsorption isotherms of both proteins on various adsorbents were also measured, thus allowing us to calculate the. . . adsorbents was exothermic, while their adsorption on octyl ones was endothermic. In addition, binding of both proteins with the butyl **ligand** is basically an adsorption process, while binding with the octyl **ligand** is adsorption and partition processes. Moreover, on both butyl or octyl, the adsorption enthalpy became increasingly positive as the **ligand** density increased, while the adsorption entropy became more positive as the alkyl chain length or density of the adsorbent increased.. . .

CT Medical Descriptors:
*chromatography
*molecular interaction
microcalorimetry
protein binding
hydrophobicity
adsorption
enthalpy
thermodynamics
article
priority journal
*M protein
***ligand**
chymotrypsinogen
trypsinogen

```
=> s (captur### or attach###)(10a)ligand#
         21826 CAPTUR###
         41728 ATTACH###
        116643 LIGAND#
L11        476 (CAPTUR### OR ATTACH###)(10A)LIGAND#

=> s l11 and (opposite(10a)charge#)
        333027 l11
         37901 OPPOSITE
         61087 CHARGE#
           370 OPPOSITE(10A)CHARGE#
L12         10 l11 AND (OPPOSITE(10A)CHARGE#)

=> s l12 and nucleic acid
         31324 "NUCLEIC"
       1190986 "ACID"
         26661 NUCLEIC ACID
                 ("NUCLEIC"(W)"ACID")
L13          0 L12 AND NUCLEIC ACID

=> dup rem l12
PROCESSING COMPLETED FOR L12
L14         10 DUP REM L12 (0 DUPLICATES REMOVED)

=> s l12 and (polynucleotide# or nucleotide#)
          3594 POLYNUCLEOTIDE#
        210163 NUCLEOTIDE#
L15          0 L12 AND (POLYNUCLEOTIDE# OR NUCLEOTIDE#)

=> d l14 1-10 bib ab kwic

L14  ANSWER 1 OF 10  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
```

AN 2003224272 EMBASE
TI Testing of the additivity-based protein sequence to reactivity algorithm.
AU Qasim M.A.; Lu W.; Lu S.M.; Ranjbar M.; Yi Z.; Chiang Y.-W.; Ryan K.; Anderson S.; Zhang W.; Qasim S.; Laskowski Jr. M.
CS M. Laskowski Jr., Department of Chemistry, Purdue University, Brown Building, 560 Oval Drive, West Lafayette, IN 47907-2038, United States. michael.laskowski.1@purdue.edu
SO Biochemistry, (3 Jun 2003) 42/21 (6460-6466).
Refs: 28
ISSN: 0006-2960 CODEN: BICHAW
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB The standard free energies of association (or equilibrium constants) are predicted for **11** multiple variants of the turkey ovomucoid third domain, a member of the Kazal family of protein inhibitors, each interacting with six selected enzymes. The equilibrium constants for 38 of 66 possible interactions are strong enough to measure, and for these, the predicted and measured free energies are compared, thus providing an additional test of the additivity-based sequence to reactivity algorithm. The test appears to be unbiased as the **11** variants were designed a decade ago to study furin inhibition and the specificity of furin differs greatly from the specificities of our six target enzymes. As the contact regions of these inhibitors are highly positive, nonadditivity was expected. Of the **11** variants, one does not satisfy the restriction that either P2 Thr or P(1)' Glu should be present and all three measurable results on it, as expected, are nonadditive. For the remaining 35 measurements, 22 are additive, 12 are partially additive, and only one is (slightly) nonadditive. These results are comparable to those obtained for a set of 398 equilibrium constants for natural variants of ovomucoid third domains. The expectation that clustering of charges would be nonadditive is modified to the expectation that major nonadditivity will be observed only if the combining sites in both associating proteins involve large **charge** clusters of the **opposite** sign. It is also shown here that an analysis of a small variant set can be accomplished with a smaller subset, in this case 13 variants, rather than the whole set of 191 members used for the complete algorithm.
AB The standard free energies of association (or equilibrium constants) are predicted for **11** multiple variants of the turkey ovomucoid third domain, a member of the Kazal family of protein inhibitors, each interacting with. . . thus providing an additional test of the additivity-based sequence to reactivity algorithm. The test appears to be unbiased as the **11** variants were designed a decade ago to study furin inhibition and the specificity of furin differs greatly from the specificities. . . of our six target enzymes. As the contact regions of these inhibitors are highly positive, nonadditivity was expected. Of the **11** variants, one does not satisfy the restriction that either P2 Thr or P(1)' Glu should be present and all three. . . to the expectation that major nonadditivity will be observed only if the combining sites in both associating proteins involve large **charge** clusters of the **opposite** sign. It is also shown here that an analysis of a small variant set can be accomplished with a smaller. . .

L14 ANSWER 2 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2002389184 EMBASE
TI NMR structure of a minimum activity domain of human parathyroid peptide hormone: Structural origin of receptor activation.
AU Jung J.; Lim S.-K.; Kim Y.; Lee W.
CS W. Lee, Department of Biochemistry, College of Science, Yonsei University, Seodaemoon-Gu, 134 Shinchon-Dong, Seoul 120-749, Korea, Republic of. wlee@spin.yonsei.ac.kr

SO Journal of Peptide Research, (1 Nov 2002) 60/5 (239-246).
Refs: 41
ISSN: 1397-002X CODEN: JPERFA
CY United Kingdom
DT Journal; Article
FS 003 Endocrinology
029 Clinical Biochemistry
LA English
SL English
AB Parathyroid hormone (PTH) which increases osteoblast numbers and bone formation by activating bone-lining cells to osteoblasts plays an important role in calcium and phosphate homeostasis and bone remodeling by activating PTH receptors. To determine the structural origin of a minimum activity domain of hPTH, we initiated a detailed structural determination of the hPTH(H14) in aqueous solution using NMR spectroscopy. Circular dichroism and NMR data demonstrated that hPTH(H14) maintains a typical helical conformation in both membrane-mimicking environments and 30% TFE solution. The solution structure clearly showed that the residues from Ser(3) to Leu(**11**) of hPTH(H14) formed a stable helical structure, especially having **charged** side-chains oriented in **opposite** directions relative to one another for optimum interaction with the receptor molecule.
AB . . . conformation in both membrane-mimicking environments and 30% TFE solution. The solution structure clearly showed that the residues from Ser(3) to Leu(**11**) of hPTH(H14) formed a stable helical structure, especially having **charged** side-chains oriented in **opposite** directions relative to one another for optimum interaction with the receptor molecule.

L14 ANSWER 3 OF 10 EMBASE
on STN
AN 2002361232 EMBASE
TI Changes in the retinal transition dipole moment in bacteriorhodopsin of the purple membrane of Halobacterium Salinarium at the so-called PH(rev).
AU Mostafa H.I.A.
CS H.I.A. Mostafa, Department of Biophysics, Faculty of Science, Cairo University, Giza, Egypt. hamszil@yahoo.com
SO Journal of Biochemistry, Molecular Biology and Biophysics, (2002) 6/1 (59-64).
Refs: 37
ISSN: 1025-8140 CODEN: JBMBF6
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
LA English
SL English
AB The chromophore transition dipole moment of light-adapted wild-type bacteriorhodopsin (WT-bR) in suspension is evaluated for pH range of 2.8-12. Significant variations in the transition dipole moment are observed at the so-called pH(rev). The results have reported a value of **11** and 8.5 Debye for chromophore transition dipole moment of the neutral purple and acid blue form of bacteriorhodopsin, respectively. There may be a correlation with the process of reversing the direction of the permanent electric dipole moment, due to the reversal of the surface **charge** asymmetry, of the purple membrane to its **opposite** side at that pH(rev).
AB . . . Significant variations in the transition dipole moment are observed at the so-called pH(rev). The results have reported a value of **11** and 8.5 Debye for chromophore transition dipole moment of the neutral purple and acid blue form of bacteriorhodopsin, respectively. There. . . with the process of reversing the direction of the permanent electric dipole moment, due to the reversal of the surface **charge** asymmetry, of the purple membrane to its **opposite** side at that pH(rev).

L14 ANSWER 4 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2001000991 EMBASE
TI Influence of desialylation on the interaction of red blood cells with a hemotoxic partly quaternized tertiary polyamine.
AU Moreau E.; Chapon P.; Vert M.; Domurado D.
CS D. Domurado, Ctr. Rech. Biopolymeres Artificiels, UMR 5473 CNRS, Universite Montpellier 1, 34060 Montpellier Cedex 2, France. domurado@pharma.univ-montp1.fr
SO Journal of Bioactive and Compatible Polymers, (2000) 15/6 (447-467). Refs: 25
ISSN: 0883-9115 CODEN: JBCPEV
CY United States
DT Journal; Article
FS 037 Drug Literature Index
052 Toxicology
LA English
SL English
AB Partly quaternized poly[thio-1-(N,N-diethyl-aminomethyl)ethylene] polycations (Q-P(TDAE)(x)) interact electrostatically with the membrane of human red blood cells (RBC) and are highly toxic when given intravenously (i.v.). In order to study the influence of sialic acid negative charges on the hemagglutination and hemolysis induced by Q-P(TDAE)(**11**), RBC were desialylated using neuraminidase. Desialylation had little influence on Q-P(TDAE)(**11**)-induced agglutination. It was concluded that this feature resulted from two **opposite** phenomena consecutive to the decrease of the negative **charge** of the cell membrane. The first was a decrease of electrostatic attraction between Q-P(TDAE)(**11**) and RBC resulting in less aggregation. The second was reduction of electrostatic repulsions between RBC, which made RBC clustering relatively easier, thus counteracting the first effect. On the other hand, the hemolyzing effect of Q-P(TDAE)(**11**) on desialyated RBC was lower than that observed for native RBC in the presence of serum and plasma, whereas it was greater in a protein-free model medium. This study confirmed that electrostatic interactions between polyanionic RBC and polycations are one of the crucial determinants, but not the only one, for polycation-induced perturbations of RBC. Among these effects, massive hemagglutination is likely to be responsible for the embolism and the ensuing animal death previously observed soon after the i.v. administration of Q-P(TDAE)(12) solutions.
AB . . . intravenously (i.v.). In order to study the influence of sialic acid negative charges on the hemagglutination and hemolysis induced by Q-P(TDAE)(**11**), RBC were desialylated using neuraminidase. Desialylation had little influence on Q-P(TDAE)(**11**)-induced agglutination. It was concluded that this feature resulted from two **opposite** phenomena consecutive to the decrease of the negative **charge** of the cell membrane. The first was a decrease of electrostatic attraction between Q-P(TDAE)(**11**) and RBC resulting in less aggregation. The second was reduction of electrostatic repulsions between RBC, which made RBC clustering relatively easier, thus counteracting the first effect. On the other hand, the hemolyzing effect of Q-P(TDAE)(**11**) on desialyated RBC was lower than that observed for native RBC in the presence of serum and plasma, whereas it. . .

L14 ANSWER 5 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1999230729 EMBASE
TI Regulatory features of the trp operon and the crystal structure of the trp RNA-binding attenuation protein from Bacillus stearothermophilus.
AU Chen X.-P.; Antson A.A.; Yang M.; Li P.; Baumann C.; Dodson E.J.; Dodson G.G.; Gollnick P.
CS P. Gollnick, Department of Biological Sciences, State University of New York, Buffalo, NY 14260, United States. gollnick@ubunix.acsu.buffalo.edu

SO Journal of Molecular Biology, (1999) 289/4 (1003-1016).
Refs: 51
ISSN: 0022-2836 CODEN: JMOBAK
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
029 Clinical Biochemistry
LA English
SL English
AB Characterization of both the cis and trans-acting regulatory elements indicates that the Bacillus stearothermophilus trp operon is regulated by an attenuation mechanism similar to that which controls the trp operon in Bacillus subtilis. Secondary structure predictions indicate that the leader region of the trp mRNA is capable of folding into terminator and anti-terminator RNA structures. B. stearothermophilus also encodes an RNA binding protein with 77% sequence identity with the RNA-binding protein (TRAP) that regulates attenuation in B. subtilis. The X-ray structure of this protein has been determined in complex with L-tryptophan at 2.5 .ANG. resolution. Like the B. subtilis protein, B. stearothermophilus TRAP has **11** subunits arranged in a ring-like structure. The central cavities in these two structures have different sizes and **opposite charge** distributions, and packing within the B. stearothermophilus TRAP crystal form does not generate the head-to-head dimers seen in the B. subtilis protein, suggesting that neither of these properties is functionally important. However, the mode of L-tryptophan binding and the proposed RNA binding surfaces are similar, indicating that both proteins are activated by L-tryptophan and bind RNA in essentially the same way. As expected, the TRAP:RNA complex from B. stearothermophilus is significantly more thermostable than that from B. subtilis, with optimal binding occurring at 70.degree.C.
AB . . . has been determined in complex with L-tryptophan at 2.5 .ANG. resolution. Like the B. subtilis protein, B. stearothermophilus TRAP has **11** subunits arranged in a ring-like structure. The central cavities in these two structures have different sizes and **opposite charge** distributions, and packing within the B. stearothermophilus TRAP crystal form does not generate the head-to-head dimers seen in the B.. . .

L14 ANSWER 6 OF 10 EMBASE
on STN
AN 96255181 EMBASE
DN 1996255181
TI Kinetic analysis of synthetic analogues of linear-epitope peptides of glycoprotein D of herpes simplex virus type 1 by surface plasmon resonance.
AU Lasonder E.; Schellekens G.A.; Koedijk D.G.A.; Damhof R.A.; Welling-Wester S.; Feijlbrief M.; Scheffer A.J.; Welling G.W.
CS Department Medical Microbiology, University of Groningen, Hanzeplein 1,9713 GZ Groningen, Netherlands
SO European Journal of Biochemistry, (1996) 240/1 (209-214).
ISSN: 0014-2956 CODEN: EJBCAI
CY Germany
DT Journal; Article
FS 004 Microbiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB The interaction between mAb A16 and glycoprotein D (gD) of herpes simplex virus type 1 was analyzed by studying the kinetics of binding with a surface-plasmon-resonance biosensor. mAb A16 belongs to group VII antibodies, which recognize residues **11**-19 of gD. In a previous study,three critical residues, Asp13, Arg16 and Phe17, of this epitope were identified by screening a phage display library that contained a

random 15-amino-acid insert with the antibody. The contribution to binding of these residues in the motif DXXRF was further analyzed by an amino-acid-replacement study of the epitope gD-(9-19)-peptide and of a gD-(9-19)-peptide mimotope, previously obtained by screening the phage display library. Amino acid residues of the motif were replaced by a neutral amino acid residue, an amino acid residue with **opposite charge** and a corresponding D-amino acid residue. Kinetic parameters of peptide analogues were determined with a surface plasmon-resonance biosensor. The kinetic parameters of the peptide analogues were compared with the kinetic parameters of the interaction between mAb A16 and the epitope gD-(9-19)-peptide. The minimal size of the go epitope for mAb A16 was also determined in this study. The kinetic constants of the resulting gD-(**11**-17)-peptide were found to be similar to those of entire go. The kinetic analysis precisely defined the epitope on go for mAb A16 to residues **11**-17, identified Arg16 as an essential residue and suggested that Asp13 and Phe17 are mainly involved in stabilization of the secondary structure of the peptide.

AB . . . by studying the kinetics of binding with a surface-plasmon-resonance biosensor. mAb A16 belongs to group VII antibodies, which recognize residues **11**-19 of gD. In a previous study,three critical residues, Asp13, Arg16 and Phe17, of this epitope were identified by screening a. . . library. Amino acid residues of the motif were replaced by a neutral amino acid residue, an amino acid residue with **opposite charge** and a corresponding D-amino acid residue. Kinetic parameters of peptide analogues were determined with a surface plasmon-resonance biosensor. The kinetic. . . size of the go epitope for mAb A16 was also determined in this study. The kinetic constants of the resulting gD-(**11**-17)-peptide were found to be similar to those of entire go. The kinetic analysis precisely defined the epitope on go for mAb A16 to residues **11**-17, identified Arg16 as an essential residue and suggested that Asp13 and Phe17 are mainly involved in stabilization of the secondary. . .

L14 ANSWER 7 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 95349710 EMBASE

DN 1995349710

TI Complexes between chaperonin GroEL and the capsid protein of bacteriophage HK97.

AU Ding Y.-H.; Duda R.L.; Hendrix R.W.; Rosenberg J.M.

CS Department of Biological Sciences, University of Pittsburgh,Pittsburgh, PA 15260, United States

SO Biochemistry, (1995) 34/45 (14918-14931).
ISSN: 0006-2960 CODEN: BICHAW

CY United States

DT Journal; Article

FS 004 Microbiology
029 Clinical Biochemistry

LA English

SL English

AB The 42 kDa capsid protein of bacteriophage HK97 requires the GroEL and GroES chaperonin proteins of its Escherichia coli host to facilitate correct folding, both in vitro and in vitro. In the absence of GroES and ATP, denatured gp5 forms a stable complex with the 14 subunit GroEL molecule. We characterized the electrophoretic and biochemical properties of this complex. In electrophoresis on a native (nondenaturing) gel, the band of the gp5- GroEL complex shifts to a slower migrating position relative to uncomplexed GroEL. The results show that there is only one subunit of gp5 bound to each GroEL 14-mer and that the shift in band position is due primarily to a change in the overall charge of the complex relative to uncomplexed GroEL, and not to a change in size or shape. GroEL forms similar complexes with proteolytic fragments of gp5, with a series of sequence duplication derivatives of gp5, and with other proteins. Electrophoretic examination of these complexes shows that a band shift

occurs with proteins larger than 31-33 kDa but not with smaller proteins. For those proteins that cause a band shift upon complex formation, the magnitude of the shift is correlated with the predicted negative charge on the protein; paradoxically, the direction of the band shift is **opposite** to what is predicted if the **charge** of the complex were simply the sum of the charge of GroEL and the charge of the substrate protein. We suggest thai binding of a substrate protein to GroEL is accompanied by a net binding of solution cations to the complex, but only in the case of proteins above a minimum size of 31-33 kDa. The gp5-GroEL complex is in an association/dissociation equilibrium, with a binding constant measured in the range of **11**-17 .mu.M-1.

AB . . . the shift is correlated with the predicted negative charge on the protein; paradoxically, the direction of the band shift is **opposite** to what is predicted if the **charge** of the complex were simply the sum of the charge of GroEL and the charge of the substrate protein. We. . . of 31-33 kDa. The gp5-GroEL complex is in an association/dissociation equilibrium, with a binding constant measured in the range of **11**-17 .mu.M-1.

L14 ANSWER 8 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 95201567 EMBASE

DN 1995201567

TI The influence of electrostatic interactions on partition in aqueous polyethylene glycol/dextran biphasic systems: Part II.

AU Schluck A.; Maurer G.; Kula M.-R.

CS Institut fur Enzymtechnologie, Heinrich-Heine-Univ. Dusseldorf, P.O. Box 2050,D-52404 Julich, Germany

SO Biotechnology and Bioengineering, (1995) 47/2 (252-260). ISSN: 0006-3592 CODEN: BIBIAU

CY United States

DT Journal; Article

FS 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
037 Drug Literature Index

LA English

SL English

AB In aqueous polyethylene glycol/dextran two-phase systems, the hydrophobicity, free volume, surface tension, and interfacial tension of the phases in equilibrium were measured as a function of pH and ionic strength. These parameters were found to change with pH, but the pattern and magnitude cannot explain the unusual partition of charged macromolecules, observed previously. The electrostatic potential difference was determined by a new experimental approach based on the measurement of the pH difference between the phases at equilibrium. In polyethylene glycol/dextran systems containing sodium chloride as ionized species, the electrostatic potential is not constant in the pH range 2 to **11**. The partition behavior of charged macromolecules and its dependence on pH can be explained by the combined action of charge and phase potential. This conclusion was tested with poly- L-glutamate, which partitioned as predicted and in a pattern **opposite** to positively **charged** macromolecules.

AB . . . glycol/dextran systems containing sodium chloride as ionized species, the electrostatic potential is not constant in the pH range 2 to **11**. The partition behavior of charged macromolecules and its dependence on pH can be explained by the combined action of charge and phase potential. This conclusion was tested with poly- L-glutamate, which partitioned as predicted and in a pattern **opposite** to positively **charged** macromolecules.

L14 ANSWER 9 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 87138461 EMBASE

DN 1987138461

TI Relationships between adsorption, chemical state and fluxes of cadmium applied as Cd(NO3)2 in isolated xylem cell walls of tomato.
AU Wolterbeek H.T.
CS Interuniversitair Reactor Institute, 2629 JB Delft, Netherlands
SO J. EXP. BOT., (1987) 38/188 (419-432).
CODEN: JEBOA6
CY United Kingdom
DT Journal
FS 046 Environmental Health and Pollution Control
LA English
AB Isolated xylem cell wall pieces were applied as membranes in ion diffusion experiments. The cell walls were isolated from tomato internodes (Lycopersicon esculentum Mill, cv. Tiny Tim) and sealed in a two-compartment diffusion system. In flux and adsorption calculations, the cell wall was regarded as a leaky membrane with parallel fluxes through Donnan Free Space (DFS) and Water Free Space (WFS). During the experiments absorption into and diffusion across the walls was determined of Cd2+, applied as 115Cd(NO3)2. Flux experiments with 82Br- indicated that excluded volume effects and path tortuosity resulted in apparent WFS diffusion coefficients in the walls which were 0.012 times as high as in water. The free proton concentration in the DFS was shown to be related to a complex formation between fixed charges and Cd2+. The cell wall permeability for Cd2+ and NO3- varied with applied and absorbed concentrations, and the Cd2+ flux curve showed an inflexion point coinciding with a buffered degree of dissociation of fixed **charges** in the DFS. The necessary coupling of fluxes of **opposite charges** resulted in relatively high NO3- and small Cd2+ permeability of the DFS for strongly diluted solutions (P = 10-4 m s-1 and 10-**11** m s-1 for NO3- and Cd2+ respectively). The results demonstrate the possible regulatory effects of the cell wall in processes of ion transfer from xylem vessels, or ion uptake in plant tissues.
AB . . . absorbed concentrations, and the Cd2+ flux curve showed an inflexion point coinciding with a buffered degree of dissociation of fixed **charges** in the DFS. The necessary coupling of fluxes of **opposite charges** resulted in relatively high NO3- and small Cd2+ permeability of the DFS for strongly diluted solutions (P = 10-4 m s-1 and 10-**11** m s-1 for NO3- and Cd2+ respectively). The results demonstrate the possible regulatory effects of the cell wall in processes. . .

L14 ANSWER 10 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 74075173 EMBASE
DN 1974075173
TI Analysis of the primary structure of collagen for the origins of molecular packing.
AU Hulmes D.J.S.; Miller A.; Parry D.A.D.; et al.
CS Lab. Molec. Biophys., Dept. Zool., Univ. Oxford, United Kingdom
SO Journal of Molecular Biology, (1973) 79/1 (137-148).
CODEN: JMOBAK
DT Journal
FS 029 Clinical Biochemistry
031 Arthritis and Rheumatism
LA English
AB The amino acid sequence in the triplet region of the .alpha.1 chain of collagen was analyzed for complementary relationships that would explain the stagger of multiples of 670 .ANG. between the rod like molecules in the fibril. The analysis was done by moving the sequence of 1011 amino acids past itself and scoring for complementarity between opposing amino acids allowing a range of .+-.2 to 3 residues. It was found that interactions between amino acids of **opposite charge** and between large hydrophobic amino acids in the overlapping region between two chains are maximal when the chains are staggered by 0D, 1D, 2D, 3D and 4D, where D = 234 .+-. 1 residues. The residue repeat derived

from this value is 2.86 .+-. 0.02 .ANG.. The existence of a D separation between interacting residues was shown to be reflected in the actual distribution of large hydrophobic amino acids. Surprisingly, the distribution approximates the pattern (2D/**11**)5(D/**11**) repeated over 4.4D intervals. The regularity may arise from structural constraints imposed by supercoiling. The distribution of charged residues is less regular and does not show a well defined periodicity. However, positively charged residues tend to be near negatively charged residues, allowing intramolecular charge neutralization as well as strong intermolecular charge interactions at 0D.

AB . . . opposing amino acids allowing a range of .+-.2 to 3 residues. It was found that interactions between amino acids of **opposite charge** and between large hydrophobic amino acids in the overlapping region between two chains are maximal when the chains are staggered. . . was shown to be reflected in the actual distribution of large hydrophobic amino acids. Surprisingly, the distribution approximates the pattern (2D/**11**)5(D/**11**) repeated over 4.4D intervals. The regularity may arise from structural constraints imposed by supercoiling. The distribution of charged residues is. . .

```
=> s l12 and (polynucleotide# or nucleotide#)s l11
MISSING OPERATOR CLEOTIDE#)S L11
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l11 and nucleic acid
         31324 "NUCLEIC"
       1190986 "ACID"
         26661 NUCLEIC ACID
                 ("NUCLEIC"(W)"ACID")
L16          5 L11 AND NUCLEIC ACID

=> s l16 and (opposite (10a)charge#)
         37901 OPPOSITE
         61087 CHARGE#
           370 OPPOSITE (10A)CHARGE#
L17          0 L16 AND (OPPOSITE (10A)CHARGE#)

=> d l16 1-5 bib ab kwic

L16  ANSWER 1 OF 5  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
AN   2000193577  EMBASE
TI   Block and graft copolymers and Nanogel(TM) copolymer networks for DNA
     delivery into cell.
AU   Lemieux P.; Vinogradov S.V.; Gebhart C.L.; Guerin N.; Paradis G.; Nguyen
     H.-K.; Ochietti B.; Suzdaltseva Y.G.; Bartakova E.V.; Bronich T.K.;
     St-Pierre Y.; Alakhov V.Yu.; Kabanov A.V.
CS   P. Lemieux, Supratek Pharma Inc., Armand-Frappier Institute, 531 blvd. des
     Prairies, Laval, Que. H7V 1B7, Canada. akabanov@unmc.edu
SO   Journal of Drug Targeting, (2000) 8/2 (91-105).
     Refs: 39
     ISSN: 1061-186X  CODEN: JDTAEH
CY   United Kingdom
DT   Journal; General Review
FS   022     Human Genetics
     029     Clinical Biochemistry
LA   English
SL   English
AB   Self-assembling complexes from nucleic acids and synthetic polymers are
     evaluated for plasmid and oligonucleotide (oligo) delivery. Polycations
     having linear, branched, dendritic, block- or graft copolymer
     architectures are used in these studies. All these molecules bind to
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nucleic acids due to formation of cooperative systems of salt bonds between the cationic groups of the polycation and phosphate groups of the DNA. To improve solubility of the DNA/polycation complexes, cationic block and graft copolymers containing segments from polycations and non-ionic soluble polymers, for example, poly(ethylene oxide) (PEO) were developed. Binding of these copolymers with short DNA chains, such as oligos, results in formation of species containing hydrophobic sites from neutralized DNA-polycation complex and hydrophilic sites from PEO. These species spontaneously associate into polyion complex micelles with a hydrophobic core from neutralized polyions and a hydrophilic shell from PEO. Such complexes are very small (10-40 nm) and stable in solution despite complete neutralization of charge. They reveal significant activity with oligos in vitro and in vivo. Binding of cationic copolymers to plasmid DNA forms larger (70-200 nm) complexes, which are practically inactive in cell transfection studies. It is likely that PEO prevents binding of these complexes with the cell membranes ('stealth effect'). However **attaching** specific **ligands** to the PEO-corona can produce complexes, which are both stable in solution and bind to target cells. The most efficient complexes were obtained when PEO in the cationic copolymer was replaced with membrane-active PEO-b-poly(propylene oxide)-b-PEO molecules (Pluronic 123). Such complexes exhibited elevated levels of transgene expression in liver following systemic administration in mice. To increase stability of the complexes, NanoGel(TM) carriers were developed that represent small hydrogel particles synthesized by cross-linking of PEI with double end activated PEO using an emulsification/solvent evaporation technique. Oligos are immobilized by mixing with NanoGel(TM) suspension, which results in the formation of small particles (80 nm). Oligos incorporated in NanoGel are able to reach targets within the cell and suppress gene expression in a sequence-specific fashion. Further, loaded NanoGel particles cross-polarized monolayers of intestinal cells (Caco-2) suggesting potential usefulness of these systems for oral administration of oligos. In conclusion the approaches using polycations for gene delivery for the design of gene transfer complexes that exhibit a very broad range of physicochemical and biological properties, which is essential for design of a new generation of more effective non-viral gene delivery systems.

AB . . . cell transfection studies. It is likely that PEO prevents binding of these complexes with the cell membranes ('stealth effect'). However **attaching** specific **ligands** to the PEO-corona can produce complexes, which are both stable in solution and bind to target cells. The most efficient. . .

CT Medical Descriptors:
*gel
*gene targeting
DNA transfer
cell strain CACO 2
complex formation
emulsion
evaporation
gene repression
genetic transfection
hydrophobicity
micelle
particle size
plasmid
suspension
nonhuman
animal cell
review
priority journal
*copolymer
macrogol
nucleic acid
oligonucleotide

plasmid DNA
poloxamer
polycation
propylene oxide
solvent

L16 ANSWER 2 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1999055869 EMBASE
TI Capillary electrochromatography with novel stationary phases: II. Studies of the retention behavior of nucleosides and bases on capillaries packed with octadecyl-sulfonated-silica microparticles.
AU Zhang M.; El Rassi Z.
CS Prof. Z. El Rassi, Department of Chemistry, Oklahoma State University, Stillwater, OK 74078-3071, United States. zelrassi@biochem.okstate.edu
SO Electrophoresis, (1999) 20/1 (31-36).
Refs: 22
ISSN: 0173-0835 CODEN: ELCTDN
CY Germany
DT Journal; Conference Article
FS 029 Clinical Biochemistry
LA English
SL English
AB An octadecyl-sulfonated silica (ODSS) stationary phase specially designed for performing capillary electrochromatography (CEC) at relatively strong electroosmotic flow (EOF) proved useful for the separations of some nucleosides and bases. The ODSS stationary phase is composed of a hydrophilic, negatively charged sublayer to which a nonpolar top layer containing octadecyl **ligands** is covalently **attached**. The charged sublayer contains sulfonic acid groups which ensure a relatively strong EOF. Due to the presence of permanently charged sulfonic acid groups in the sublayer, the hydrophilic nature of the sublayer and the hydrophobic character of the top octadecyl layer, retention and selectivity of charged and relatively polar nucleosides and bases on the ODSS stationary phase are based on electrostatic interaction, hydrophilic interaction, and reversed-phase mechanisms. This yielded for the ODSS stationary phase a unique selectivity towards the nucleosides and bases, thus allowing their rapid separation. To gain insight into the chromatographic behavior of nucleosides and bases on the ODSS stationary phase, the results were compared to those obtained on an octadecyl-silica (ODS) capillary under otherwise the same elution conditions. Due to the difference in the nature of the organic layers on the surface of the ODSS and ODS stationary phases, the elution order on both stationary phases differed significantly, and the ODSS capillary proved more suitable for the separation of the nucleosides and bases than the ODS capillary.
AB . . . The ODSS stationary phase is composed of a hydrophilic, negatively charged sublayer to which a nonpolar top layer containing octadecyl **ligands** is covalently **attached**. The charged sublayer contains sulfonic acid groups which ensure a relatively strong EOF. Due to the presence of permanently charged. . .
CT Medical Descriptors:
*capillary chromatography
particle size
electroosmosis
hydrophilicity
hydrophobicity
electricity
conference paper
*nucleoside
***nucleic acid base**
*octadecylsilicon dioxide
*silicon derivative
*sulfonic acid derivative

L16 ANSWER 3 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 1998082444 EMBASE

TI FastTag(TM) **nucleic acid** labeling system: A versatile method for incorporating haptens, fluorochromes and affinity ligands into DNA, RNA and oligonucleotides.

AU Daniel S.G.; Westling M.E.; Moss M.S.; Kanagy B.D.

CS B.D. Kanagy, Vector Laboratories, Inc., 30 Ingold Road, Burlingame, CA 94010, United States. bkanag@zippy.vectorlabs.com

SO BioTechniques, (1998) 24/3 (484-489).
Refs: 14
ISSN: 0736-6205 CODEN: BTNQDO

CY United States

DT Journal; General Review

FS 027 Biophysics, Bioengineering and Medical Instrumentation
022 Human Genetics

LA English

SL English

AB The FastTag(TM) **Nucleic Acid** Labeling System couples haptens, flourochromes or affinity **ligands** to any **nucleic acid** by **attaching** a universal, photo- or heat-activatable moiety to which any sulfltydrylreactive compound can be linked. To demonstrate the versatility of the FastTag system, we have labeled DNA, RNA and oligonucleotide probes with a variety of maleimide-coupled moieties and have used these probes in several applications. In Southern hybridization analyses, RNA probes labeled using FastTag FL (fluorescein) detected 0.04 pg of target DNA. Human satellite DNA clones labeled using FastTag FL or FastTag Biotin detected the corresponding sequences in human chromosome spreads and interphase nuclei by fluorescence in situ hybridization. An antisense oligonucleotide probe cocktail complementary to human proinsulin transcripts labeled using FastTag DNP (dinitrophenyl) detected, in situ, the appropriate transcripts in pancreatic tissue sections. Oligonucleotide primers labeled with FastTag FL were used to PCR-amplify a genomic DNA fragment, which was then detected immunologically. Finally, we discurs how DNA labeled with FastTag Fucose can be bound to a fucose-binding affinity matrix and eluted under mild conditions.

TI FastTag(TM) **nucleic acid** labeling system: A versatile method for incorporating haptens, fluorochromes and affinity ligands into DNA, RNA and oligonucleotides.

AB The FastTag(TM) **Nucleic Acid** Labeling System couples haptens, flourochromes or affinity **ligands** to any **nucleic acid** by **attaching** a universal, photo- or heat-activatable moiety to which any sulfltydrylreactive compound can be linked. To demonstrate the versatility of the. . .

CT Medical Descriptors:
*genetic analysis
*molecular probe
southern blotting
fluorescence in situ hybridization
dna sequence
molecular cloning
chromosome analysis
gene amplification
polymerase chain reaction
pancreas
rna probe
dna probe
oligonucleotide probe
human
human tissue
human cell
review
***nucleic acid**

*hapten
*fluorochrome
*dna
*rna
*oligonucleotide
*proinsulin
ligand
thiol derivative

NP **(1) FastTag Nucleic Acid Labeling System**; (2) Riboprobe In Vitro Transcription System; (3) Texas Red; (4) PHOTOPROBE

L16 ANSWER 4 OF 5 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 96280804 EMBASE

DN 1996280804

TI Solution conformation of the (-)-cis-anti-benzo[a]pyrenyl-dG adduct opposite dC in a DNA duplex: Intercalation of the covalently attached BP ring into the helix with base displacement of the modified deoxyguanosine into the major groove.

AU Cosman M.; Hingerty B.E.; Luneva N.; Amin S.; Geacintov N.E.; Broyde S.; Patel D.J.

CS Cellular Biochemistry/Biophys. Prog., Memorial Sloan Kettering Cancer Ctr.,New York, NY 10021, United States

SO Biochemistry, (1996) 35/30 (9850-9863).
ISSN: 0006-2960 CODEN: BICHAW

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English

SL English

AB This paper reports on the combined NMR-molecular mechanics computational studies of the solution structure of the (-)-cis-anti-[BP]dG adduct positioned opposite dC in the sequence context d(C1-C2-A3-T4-C5-[BP]G6-C7-T8-A9-C10-C11).cntdot.d(G12-G13-T14-A15-G16-C17-G18-A19-T20-G21-G22) duplex [designated (-)-cis-anti-[BP]dG.cntdot.dC 11-mer duplex]. This adduct is derived from cis addition at C10 of (-)-anti-7(S),8(R)-dihydroxy-9(R), 10(S)- epoxy-7,8,9,10-tetrahydrobenzo[a]pyrene [(-)-anti-BPDE] to the N2 position of dG6 in this duplex sequence. The exchangeable and nonexchangeable protons of the benzo[a]pyrenyl moiety and **nucleic acid** of the major conformation were assigned following analysis of two-dimensional NMR data sets in H2O and D2O solution. There was a general broadening of proton resonances for a three- nucleotide segment centered about the lesion site which resulted in a tentative assignment for the sugar protons of the C7 residue in the spectrum of the adduct duplex. The solution conformation of the major conformation of the (-)-cis-anti-[BP]dG.cntdot.dC 11-mer duplex has been determined by incorporating DNA-DNA and intermolecular BP-DNA proton-proton distances defined by lower and upper bounds deduced from NOESY data sets as restraints in molecular mechanics computations in torsion angle space. The results establish that the covalently attached benzo[a]pyrenyl ring intercalates between intact Watson-Crick dC5.cntdot.dG18 and dC7.cntdot.dG16 base pairs. The modified deoxyguanosine [BP]-dG6 and its partner cytosine dC17 are looped out of the helix into the major groove. The purine ring of the [BP]dG6 residue is directed toward the 5'-end of the modified strand and stacks over the major groove edge of its 5'-side neighbor dC5 residue. The solution structure of the (-)-cis-anti-[BP]dG.cntdot.dC 11-mer duplex is compared with those of the stereoisomeric (+)-trans-anti-[BP]dG [Cosman, M., et al. (1992) Proc. Natl. Acad. Sci. U.S.A. 89, 1914-1918], (-)-trans-anti-[BP]dG [de los Santos, C., et al. (1992) Biochemistry 31, 5245-5252], and (+)-cis-anti-[BP]dG [Cosman, M., et al. (1993a) Biochemistry 32, 4146-4155] adducts positioned opposite dC in the same duplex sequence context. A key finding is that the long axes of the intercalated benzo[a]pyrenyl rings in the solution structures of the (+)- and

(-)-cis-anti-[BP]dG.cntdot.dC 11-mer duplexes are oriented in opposite directions with the benzylic ring directed toward the minor groove in the (+)-cis isomer and toward the major groove in the (-)-cis isomer. In addition, a comparison is also made with the solution structure of the (+)- trans-anti-[BP]dG adduct opposite a deletion site [Cosman, M., et al. (1994a) Biochemistry 33, 11507-11517] since this adduct duplex displays several conformational features in common with the structure of the (-)-cis-anti- [BP]dG.cntdot.dC 11-mer duplex. The structures of both duplex adducts exhibit intercalation of the covalently **attached ligand** into the helix and displacement of the modified deoxyguanosine into the major groove. Studies of the biological activities of stereochemically defined BP-DNA adducts and the comparison of the solution structure of the (-)-cis-anti-[BP]dG.cntdot.dC 11-mer duplex with its stereoisomeric counterparts should lead to new insights into the relationships between defined helical distortions and mutagenic specificity and activity.

AB . . . to the N2 position of dG6 in this duplex sequence. The exchangeable and nonexchangeable protons of the benzo[a]pyrenyl moiety and **nucleic acid** of the major conformation were assigned following analysis of two-dimensional NMR data sets in H2O and D2O solution. There was. . . with the structure of the (-)-cis-anti-[BP]dG.cntdot.dC 11-mer duplex. The structures of both duplex adducts exhibit intercalation of the covalently **attached ligand** into the helix and displacement of the modified deoxyguanosine into the major groove. Studies of the biological activities of stereochemically. .

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AN 80148777 EMBASE

DN 1980148777

TI Hydrophobic affinity chromatography of nucleic acids and proteins.

AU Cashion P.; Sathe G.; Javed A.; Kuster J.

CS Biol. Dept., Univ. New Brunswick, Fredericton E3B 5A3, Canada

SO Nucleic Acids Research, (1980) 8/5 (1167-1185).
CODEN: NARHAD

CY United Kingdom

DT Journal

FS 029 Clinical Biochemistry

LA English

AB 5' tritylated oligonucleotides binding hydrophobically to low trityl cellulose/sepharose (<15.mu.MTr/ml) retain their hydrogen-bonding specificities for complementary sequences. This, constitutes a novel mode of **attaching** affinity **ligands** to solid supports, is more convenient than existing methods, and proceeds with 100% yield. The salt, dielectric constant and temperature dependance of these non-covalently anchored ligands permits the isolation of a variety of RNAs including fibroin mRNA. Medium trityl sepharose (15-40.mu.M Tr/ml) has a high binding specificity for poly A and poly A containing mRNA, equivalent to dT cellulose. Most proteins, including **nucleic acid** enzymes, bind to these columns and retain enzymatic activity, thus mimicking enzymes attached covalently to solid phases. A number of in vivo counterparts to this hydrophobically determined specificity are noted, as are homologies to nitro-cellulose filters.

AB . . . binding hydrophobically to low trityl cellulose/sepharose (<15.mu.MTr/ml) retain their hydrogen-bonding specificities for complementary sequences. This, constitutes a novel mode of **attaching** affinity **ligands** to solid supports, is more convenient than existing methods, and proceeds with 100% yield. The salt, dielectric constant and temperature. . . has a high binding specificity for poly A and poly A containing mRNA, equivalent to dT cellulose. Most proteins, including **nucleic acid** enzymes, bind to these columns and retain enzymatic activity, thus mimicking enzymes attached covalently to solid phases. A number of. . .

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CT   Medical Descriptors:
     methodology
     *messenger rna
       *nucleic acid
     *protein
     fibroin
     radioisotope


=> s opposite(10a)charge#
         37901 OPPOSITE
         61087 CHARGE#
L18        370 OPPOSITE(10A)CHARGE#

=> s l18 and captur###
         21826 CAPTUR###
L19          3 L18 AND CAPTUR###

=> s l19  and nucleic acid
         31324 "NUCLEIC"
       1190986 "ACID"
         26661 NUCLEIC ACID
                 ("NUCLEIC"(W)"ACID")
L20          0 L19 AND NUCLEIC ACID

=> d hit
L20 HAS NO ANSWERS
L18         370 SEA FILE=EMBASE OPPOSITE(10A)CHARGE#
L19           3 SEA FILE=EMBASE L18 AND CAPTUR###
L20           0 SEA FILE=EMBASE L19 AND NUCLEIC ACID


=> hit
HIT IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=>
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